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UPDATE

Vision-related quality of life and choroidal neovascular age-related macular degeneration

Qualidade de vida relacionada à visão e forma neovascular coroidal de degeneração macular relacionada à idade

Calidad de vida relacionada a la visión y forma neovascular coroidal de degeneración macular asociada a la edad

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ABSTRACT

Objective: To describe the impact of choroidal neovascular age-related macular degeneration (nAMD) on vision-related quality of life (VRQoL) in a sample of Brazilian patients, demonstrate the ability of the NEI-VFQ 25 to evaluate the impact of treatment for nAMD on VRQoL, and make recommendations for incorporating the NEI-VFQ 25 into routine clinical practice. **Methods:** This observational clinical study included 87 patients clinically diagnosed with nAMD between September 2013 and November 2016 at three ophthalmology referral centers in São Paulo and Paraná (Brazil). At the end of the treatment, a validated Portuguese-language version of the NEI-VFQ 25 was self-administered, covering 12 domains. The findings were correlated with age, gender, disease laterality, and best-corrected visual acuity (VA) of the best eye and the worst eye. **Results:** All the measured variables affected VRQoL, especially laterality, followed by age and gender. VA of the best eye significantly affected the greatest number of domains. In contrast, VA of the worst eye was nonsignificant in all domains. **Conclusions:** In nAMD patients, maintaining VA (Snellen) ≥0.5 in the best eye is essential for sustained VRQoL, regardless of VA in the worst eye. The incorporation of the NEI-VFQ 25 into routine clinical practice is strongly recommended.

Keywords: Macular degeneration; Quality of life; Assessment; Chronic disease.

RESUMO

Objetivo: Descrever o impacto de degeneração macular choroidal neovascular relacionada à idade (*n*AMD) sobre a qualidade de vida visual (QVV) em uma amostra de pacientes brasileiros, demonstrar a relevência do questionário NEI-VFQ 25 à avaliação do impacto do tratamento para *n*AMD sobre a QVV, e fazer recomendações para a incorporação do NEI-VFQ 25 à rotina clínica. **Métodos:** O presente estudo observacional incluiu 87 pacientes diagnosticados clinicamente com *n*AMD entre setembro de 2013 e novembro de 2016 em três centros de oftalmologia em São Paulo e Paraná. Ao fim do tratamento, o NEI-VFQ 25 (validado para a língua portuguesa) foi auto-aplicado, cobrindo 12 domínios. Os achados foram correlacionados com idade, gênero, lateralidade e acuidade visual (AV) no melhor e no pior olho. **Resultados:** Todas as variáveis mensuradas influenciaram a QVV, especialmente a lateralidade, seguida por idade e gênero. A AV do melhor olho foi a variável que influenciou significativamente o maior número de domínios relacionados à QVV; já a AV do pior olho não foi significante para nenhum domínio. **Conclusões:** Em pacientes com *n*AMD, a manutenção de uma AV (Snellen) de ≥0.5 no melhor olho é fundamental para uma QVV sustentada, independentemente da AV no pior olho. A incorporação do NEI-VFQ 25 à rotina clínica é fortemente recomendada.

Palavras-chave: Degeneração Macular; Qualidade de vida; Doença crônica.

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RESUMEN

Objetivo: Describir el influjo de la degeneración macular coroidal neovascular asociada a la edad (*n*AMD) sobre la cualidad de vida visual (QVV) en una amuestra de pacientes brasileños, demonstrar la relevancia de la encuesta NEI-VFQ 25 para la evaluación del impacto de la terapia para la *n*AMD sobre la QVV, además de hacerse recomendaciones a la incorporación de la encuesta NEI-VFQ 25 a la rutina clínica. **Métodos:** el presente estudio de observación incluye 87 pacientes diagnosticados clínicamente con *n*AMD entre los meses de septiembre de 2013 y noviembre de 2016 en tres centros de oftalmología en São Paulo y en Paraná. Al fin del tratamiento, la NEI-VFQ 25 (validada para la lengua portuguesa) fue aplicada de manera personal, alcanzando 12 dominios. Las respuestas encontradas se han correlacionado con edad, género, lateralidad y acuidad visual (AV) en el mejor y en el peor ojo. **Resultados:** Todas las variables medidas influenciaron la QVV, sobretodo la lateralidad, seguida por edad y género. La AV del mejor ojo fue la variable que influyó significativamente un número más grande de dominios relacionados a la QVV; ya la AV del peor ojo no mostró resultado significante para ningún de los dominios. **Conclusiones:** En pacientes con *n*AMD, la manutención de una AV (Snellen) de ≥0.5 en el mejor ojo es fundamental para una QVV que se sostenga, independientemente de la AV en el peor ojo. La incorporación de la NEI-VFQ 25 a la rutina clínica se recomienda fuertemente.

Palabras Clave: Degeneración Macular; Calidad de Vida; Enfermedad Crónica.

INTRODUCTION

The Brazilian population is aging rapidly. In fact, Brazil now boasts having the world's sixth-largest absolute number of citizens over 60 years of age[1,2]. This age range is associated with a significant increase in chronic degenerative diseases, including age-related macular degeneration (AMD)—the primary factor responsible for the severe and irreversible loss of visual acuity (VA)[3]. In its early stage, AMD is characterized by drusen and pigmentary changes, while late-stage AMD is classified into two subtypes: geographic atrophy and choroidal neovascularization (*n*AMD)[4]. Although only 10%–20% of AMD cases are classified as *n*AMD, this subtype accounts for 80%–90% of AMD-related blindness[5].

Visual loss is correlated with morbidity and mortality in the elderly due to both the increased risk of falls, disability, and depression, and greater difficulty with daily activities[6-9]. In this scenario, VA is not as reliable a parameter of visual impairment[8,9] as is vision-related quality of life (VRQoL). The latter may be quantified with the National Eye Institute Visual Functioning Questionnaire 25 (NEI-VFQ 25), with emphasis on daily activities[6-11].

Antiangiogenic therapy [intravitreal administration of vascular endothelial growth factor (VEGF) inhibitors] is currently the treatment of choice for *n*AMD[12-17]. However, due to its prohibitive cost, access to treatment is limited in public healthcare. Improving the access of *n*AMD patients to antiangiogenic therapy in the Brazilian public health setting requires addressing a range of ethical and bioethical resource allocation issues. This strategy would make little sense unless it could be shown that the rehabilitation of *n*AMD patients had a significant influence on their VRQoL.

The primary objective of this study was to describe the impact of treatment for *n*AMD on VRQoL in a sample of Brazilian patients, explore the association between VRQoL and the parameters age, sex, and laterality, and determine the importance of VA of both the best eye (VA-BE) and the worst eye (VA-WE). The secondary objective was to assess the ability of the NEI-VFQ 25 to evaluate the impact of antiangiogenic therapy on VRQoL and make recommendations for incorporating the NEI-VFQ 25 into routine clinical practice.

METHODS

The sample of this observational clinical study consisted of 87 *n*AMD patients of both genders who submitted to retinal evaluation at three Brazilian ophthalmology referral centers—two in São Paulo (Araras; São José do Rio Preto), and one in Paraná (Londrina)—between September 2013, and November 2016.

Patient eligibility requirements for the study included that they give their informed written consent, be at least 50 years old, and have a clinical diagnosis of *n*AMD confirmed by optical coherence tomography and retinography. Also, they must follow the treat-and-extend protocol outlined in the LUCAS trial[14] or the PrONTO protocol[16], using aflibercept (Eylea®, Regeneron Pharmaceuticals Inc., Rensselaer, USA) or ranibizumab (Lucentis®, Novartis Pharma Stein AG, Stein, Switzerland).

Patients were excluded who had less than one year of follow-up or a history of non-AMD-related ocular disease potentially compromising VA (i.e., uncontrolled glaucoma, ischemic optic neuropathy, clinically significant

diabetic macular edema, proliferative diabetic retinopathy, active uveitis, angioid streaks, signs of myopic choroiditis, and refraction greater than -8 D on the most recent prescription).

Study parameters included age, gender, number of anti-VEGF injections received, disease laterality, and best-corrected VA (Snellen) at the last follow-up visit.

The protocol was approved by the Research Ethics Committee of the University of São Paulo Medical School and filed under entry #253/2015.

NEI-VFQ 25

At the end of treatment, a validated, Portuguese-language version of the NEI-VFQ 25[18] was self-administered that covered 12 domains: general health, general vision, ocular pain, near activities, distance activities, vision-related social function, vision-related mental health, vision-related role difficulties, vision-related dependency, driving, color vision, and peripheral vision. The total score was calculated by averaging the 12 domains and ranged from 0 (worst possible function) to 100 (best possible function)[18].

Cronbach's alpha coefficients were calculated to evaluate the consistency and reliability of answers. A coefficient of ≥0.70 is recommended, although values above 0.60 are widely accepted in the literature[19].

Associations between scores and dichotomous variables, such as gender (male/female) and laterality (unilateral/bilateral), were analyzed with the Mann-Whitney test. Associations with stratified age (<75 years; 75–84 years; >84 years) were evaluated with the Kruskal–Wallis test. Following confirmation of the assumption of homogeneity of variance and normality using scatter charts and normal curves, respectively, the impact of VA-BE (≥0.3 and <0.3) and VA-WE (≥1.0 and <1.0) on VRQoL was determined for each domain with a two-way fixed-effects ANOVA. We evaluated the effect of each eye, both independently and dependently (BE vs. WE). All statistical analyses were performed with the software SYSTAT v.12 (Systat Software Inc., Chicago, Illinois, USA). The level of statistical significance was set at 5% ($\alpha = 0.05$).

RESULTS

Female gender was predominant in our sample of 87 Caucasian *n*AMD patients (n = 57; 65.5% vs. n = 30; 34.5%). The mean age and standard deviation was 78.4 ± 7.9 years. Age was distributed as follows: <75 years (n = 27; 31%), 75–84 years (n = 34; 39%), and >84 years (n = 26; 30%). Disease was more often unilateral than bilateral (n = 62; 72.9% vs. n = 25; 26.1%). The mean follow-up time was 76 ± 6.63 weeks. On average, patients with monocular and binocular disease received 9.2 ± 5.9 and 12.3 ± 7.9 anti-VEGF injections, respectively (overall mean: 9.84 ± 5.33). VA was 0.38 ± 0.19 (BE) and 0.13 ± 0.11 (WE).

Answers to the questionnaire met the basic criteria for internal consistency (Cronbach's alpha coefficient >0.70), except for the domains 'ocular pain' and 'driving' (0.65). No coefficients could be calculated for the domains 'general health,' 'general vision,' 'color vision,' and 'peripheral vision' since they were represented by only one question on the NEI-VFQ 25.

All scores were above 60%, except for the domain 'general health' (49.43%). Mean scores above 90% were observed for 'ocular pain' (92.96%), 'social function' (90.23%), 'color vision' (93.60%), and 'peripheral vision' (90.52%). Mean scores in the range of 70%–80% were observed for 'driving' (77.96%), 'dependency' (74.71%), and 'total score' (72.26%). Mean scores in the range of 60%–70% were observed for 'general vision' (61.84%), 'near activities' (62.06%), 'distance activities' (65.85%), 'mental health' (63.5%), and 'role difficulties' (68.82%).

Males scored better than females on all domains, except for 'driving,' but the difference was only significant for 'near activities,' 'distance activities,' 'role difficulties,' 'driving,' and 'total score' ($p < .05$) (Table 1).

Mean scores for 'role difficulties' and 'dependency' were significantly associated with age ($p < .01$) (Table 2). Thus, 'role difficulties' scores were significantly higher for younger patients (≤84 years) than for patients >84 years (Table 2). Likewise, dependency scores varied significantly between the three age groups, with patients aged <75 years scoring the highest, followed by patients aged 75–84 years, and then by patients >84 years (Table 2).

Mean scores for 'near activities,' 'distance activities,' 'social function,' 'role difficulties,' 'color vision,' 'dependency,' 'peripheral vision,' and 'total score' were significantly associated with disease laterality ($p < .01$). Thus, patients with bilateral disease had lower scores on all domains for which the association was statistically significant (Table 3).

The results of ANOVA revealed no significant interactions between BE and WE for any domain (Table 4). The impact of AV-BE was statistically significant for the dimensions 'general vision,' 'near activities,' 'distance

Table 1. Analysis of variance (*p*-values) of vision-related quality of life scores according to NEI-VFQ 25 domain and gender.

NEI-VFQ 25 domain	n	Male	n	Female	*p*-value*
General health	30	53.,33	57	47.36	0.187
General vision	30	63.33	57	61.05	0.493
Ocular pain	30	93.81	57	92.64	0.478
Near activities	30	74.21	57	55.51	**0.009**
Distance activities	30	77.86	57	59.66	**0.015**
Social function	30	93.43	57	89.17	0.122
Mental health	30	64.23	57	63.14	0.996
Role difficulties	30	79,70	57	63.29	**0.021**
Dependency	30	80.86	57	71.47	0.070
Driving	12	73.61	19	80.70	**0.030**
Color vision	30	95.83	57	92.12	0.360
Peripheral vision	30	95.01	57	87.94	0.085
Total score	30	77.71	57	69.32	**0.045**

* statistically significant at the 5% level ($p<0.05$) in bold type.

Table 2. Analysis of variance (*p*-values) of vision-related quality of life scores according to NEI-VFQ 25 domain and age group (years).

NEI-VFQ 25 domain	n	<75	n	75-84	n	>84	*p*-value*
General health	34	45.37	27	52.20	26	50.00	0.598
General vision	34	62.22	27	65.29	26	56.92	0.318
Ocular pain	34	95.92	27	91.64	26	91.88	0.433
Near activities	34	69.18	27	66.44	26	48.57	0.090
Distance activities	34	74.46	27	67.52	26	55.96	0.153
Social function	34	92.22	27	92.44	26	85.69	0.258
Mental health	34	65.30	27	66.47	26	56.76	0.152
Role difficulties	34	76.03[a]	27	74.38[a]	26	54.50[b]	**0.022**
Dependency	34	85.85[a]	27	76.00[b]	26	61.46[c]	**0.014**
Driving	15	72.20	12	84.74	4	79.17	0.606
Color vision	34	97.22	27	96.32	26	86.53	0.063
Peripheral vision	34	89.85	27	90.44	26	90.38	0.977
Total score	34	76.80	27	74.88	26	64.23	0.077

* statistically significant at the 5% level ($p<0.05$) in bold type. Values followed by different letters are significantly different ($p<0.05$). Values followed by the same letter are not significantly different ($p>0.05$).

Table 3. Analysis of variance (*p*-values) of vision-related quality of life scores according to NEI-VFQ 25 domain and disease laterality.

NEI-VFQ 25 domain	n	Unilateral disease	n	Bilateral disease	Unilateral/bilateral disease *p*-value* (Student's *t* test)
General health	62	50.00	25	48.00	0.709
General vision	62	62.90	25	59.20	0.238
Ocular pain	62	93.41	25	92.12	0.689
Near activities	62	67.11	25	49.16	**0.027**
Distance activities	62	73.08	25	48.24	**0.008**
Social function	62	92.83	25	85.20	**0.029**
Mental health	62	65.37	25	58.92	0.066
Role difficulties	62	74.58	25	55.08	**0.007**
Dependency	62	80.03	25	60.72	**0.028**
Driving	24	79.54	7	72.57	0.213
Color vision	62	97.17	25	85.00	**0.047**
Peripheral vision	62	94.37	25	80.00	**0.001**
Total score	62	76.00	25	63.08	**0.009**

* statistically significant at the 5% level ($p<0.05$) in bold type.

activities,' 'social function,' 'role difficulties,' 'dependency,' 'color vision,' 'peripheral vision,' and 'total score' ($p < .05$) (Table 4).

Table 5 shows the individual effect of BE and WE for each domain since no significant interaction between the eyes was observed. The dimensions 'general health,' 'mental health,' 'driving,' and 'ocular pain' were not significantly associated with BE and WE. The independent influence of BE (between 0.43 and -23.64) was greater in all domains, except for 'driving' (Table 5). Scores were higher for VA-BE ≥0.3 than for VA-BE <0.3. The impact of WE on VRQoL was not significant. Mean scores were more than 20% lower for WE than for BE concerning 'near activities' (-23.64%), 'distance activities' (-22.34%), and 'role difficulties' (-20.91%) (Table 5).

Table 4. Analysis of variance (*p*-values) of vision-related quality of life scores according to NEI-VFQ 25 domain and final visual acuity in the best eye (BE) and the worst eye (WE).

NEI-VFQ 25 domain	n	R^2	BE (*p*)†	WE (*p*)	BE vs. WE (*p*)
General health	87	0.01	0.802	0.351	0.949
General vision	87	0.11	**0.014**	0.825	0.117
Ocular pain	87	0.04	0.272	0.418	0.821
Near activities	87	0.08	**0.041**	0.525	0.519
Distance activities	87	0.07	**0.022**	0.932	0.662
Social function	87	0.09	**0.048**	0.178	0.236
Mental health	87	0.08	0.524	0.212	0.184
Role difficulties	87	0.09	**0.017**	0.596	0.864
Dependency	87	0.13	**0.045**	0.120	0.318
Driving	31	0.21	0.493	0.326	0.076
Color vision	87	0.05	**0.047**	0.957	0.625
Peripheral vision	87	0.06	**0.034**	0.235	0.595
Total score	87	0.09	**0.037**	0.540	0.403

† statistically significant at the 5% level (p<0.05) in bold type.

Table 5. Analysis of variance (*p*-values) of vision-related quality of life scores according to NEI-VFQ 25 domain, and VA-BE and VA-WE intervals.

NEI-VFQ 25 domain	BE<0.5	BE≥0.5	Diff	*p*	WE<0.1	WE≥0.1	Diff	*p**
General health	49.57	49.14	0.43	NS	47.67	51.14	-3.46	NS
General vision	57.24	71.03	-13.79	**S**	57.21	66.36	-9.15	NS
Ocular pain	91.38	96.12	-4.74	NS	91.28	94.60	-3.32	NS
Near activities	54.09	77.73	-23.64	**S**	52.81	61.32	-8.51	NS
Distance activities	58.41	80.75	-22.34	**S**	59.59	61.97	-2.38	NS
Social function	77.93	94.83	-16.90	**S**	90.70	89.77	0.92	NS
Mental health	61.10	67.24	-6.14	NS	57.70	58.47	-0.77	NS
Role difficulties	61.85	82.76	-20.91	**S**	61.34	66.14	-4.80	NS
Dependency	68.39	87.36	-18.97	**S**	64.73	74.47	-9.74	NS
Driving	76.00	80.00	-4.00	NS	66.67	73.33	-6.66	NS
Color vision	90.79	99.14	-8.35	**S**	91.28	95.93	-4.65	NS
Peripheral vision	87.93	95.69	-7.76	**S**	88.95	92.05	-3.09	NS
Total score	67.93	80.92	-12.98	**S**	66.70	67.70	-1.00	NS

* statistically significant at the 5% level (p<0.05) in bold type; S: significant; NS: non-significant.

DISCUSSION

The demographic profile of our sample (69% >75 years; 65.5% female) matched the normal distribution of a population of patients with AMD[5]. This fact is relevant since age can introduce bias into the interpretation of answers to questionnaires. The purpose of anti-VEGF therapy for *n*AMD is to inhibit choroidal neovascularization and maintain good vision for as long as possible. However, the situation requires a series of visits and injections[5].

The NEI-VFQ 25 was used to identify associations between low vision and poor VRQoL in *n*AMD patients. In our opinion, the NEI-VFQ 25 is the best assessment tool available for this task. In the present study, VRQoL was affected by all variables tested, although some domains were more affected by VA than others.

The domains 'distance activities,' 'near activities,' 'role difficulties,' 'driving,' and 'total score' were significantly associated with gender (Table 1), while only two domains ('role difficulties' and 'dependency') were associated with age (Table 2). In comparison, AMD patients assessed by Szlyk et al.[20] displayed poorer performance on the driving simulator, including delayed braking response times to stop signs, slower speeds, and both more lane boundary crossings and simulator accidents. AMD patients also displayed poorer overall on-road test performance, including having significantly more points deducted for driving too slowly and for not maintaining proper lane position.

Laterality was significantly associated with eight of the 12 domains on the NEI-VFQ 25 (Table 3). In these eight domains, scores were lower for patients with binocular disease. VA was the variable, which affected the greatest number of domains at statistically significant levels, i.e., the variable most strongly correlated with VRQoL. In two other studies, NEI-VFQ 25 scores were lower for binocular than for monocular AMD-related visual (vision) loss[21,22]. However, a study comparing 54 patients who had monocular blindness with 54 patients who had binocular blindness found higher levels of emotional distress in the former group, perhaps because of uncertainty regarding future disease progression[23].

Lower scores in all domains of patients with bilateral *n*AMD are in agreement with the literature[11,22]. The most considerable difference between bilateral and monocular disease was observed for 'role difficulties' and 'distance activities' (>20%). As in other vision-threatening conditions, loss of near and far vision is a major cause of the loss of VRQoL among bilateral *n*AMD patients. In one study, AMD patients who reported poor adaptation to vision loss, especially concerning acceptance of and compensation for vision loss, had more depressive symptoms than better-adapted patients[25]. Role difficulties also severely compromise VRQoL and can aggravate depression in *n*AMD patients due to inability to work[6-8]. Activities commonly affected include meal preparation, traveling, cleaning, grooming, shopping, going out, navigating both steps and pavement curbs, noticing objects, hobbies, watching TV, reading, driving (especially night driving), and using low-vision devices[26,27].

VA-BE influenced the highest number of VRQoL domains significantly, whereas VA-WE was not significant for all domains (Table 4). No significant interactions were found between BE and WE for any domain, suggesting BE and WE have independent effects on VRQoL[21,22,24].

Patients with VA-BE ≥0.3 obtained higher NEI VF-25 scores than patients with VA-BE <0.3 (Table 5). Since VA-WE had no measurable influence on VRQoL in any domain, the maintenance of VA-BE ≥0.3 appears to be essential for sustained VRQoL in this population. Likewise, Berdeaux et al.[24] found a strong correlation between VRQoL and VA-BE, suggesting the best eye be given treatment priority. This strategy is effective when VA-BE is <0.3, but the treatment of bilateral *n*AMD patients targeting only the best eye may underestimate the impact of low VA-WE on VRQoL. According to Hirneiss et al.[28], VRQoL can be sustained or improved independently of which eye is given treatment priority.

The healthcare cost of a newly diagnosed *n*AMD patient may cost approximately USD 250,000[29], a prohibitive cost in the public healthcare setting. Moreover, although currently available treatments for *n*AMD may preserve vision, they do not provide a cure for the disease. Our study shows that the maintenance of VA-BE ≥0.3 is essential for VRQoL, raising the question of whether resources and treatment for *n*AMD should be made available for both eyes, or primarily for the BE. Based on our findings, in *n*AMD patients with VA-BE <0.3, the best eye should be given priority to ensure VRQoL for as long as possible. Moreover, our study confirmed the ability of the NEI-VFQ 25 to evaluate the impact of treatment for *n*AMD on VRQoL. Thus, we strongly recommend the incorporation of this questionnaire into routine clinical assessments.

REFERENCES

1. Chaimowicz F. A saúde dos idosos brasileiros às vésperas do século XXI: problemas, projeções e alternativas. Rev Saúde Pública. 1997;31(2):184-200.
2. Macedo BG, Pereira LSM, Castro ANBV, Camelo J, Sales PCD. Correlação entre acuidade visual e desempenho funcional em idosos com catarata. Geriatr Gerontol Aging. 2009;3(4):158-63.
3. Colijn JM, Buitendijk GHS, Prokofyeva E, Alves D, Cachulo ML, Khawaja AP, et al.; EYE-RISK consortium; European Eye Epidemiology (E3) consortium. Prevalence of Age-Related Macular Degeneration in Europe: The Past and the Future. Ophthalmology. 2017;124(12):1753-63.
4. Klein R, Klein BE, Linton KL. Prevalence of age-related maculopathy: the Beaver Dam Eye Study. Ophthalmology. 1992;99(6):933-43.
5. Ávila M, Garcia JMBB, Isaac DLC. Degeneração macular relacionada à idade: presente e futuro. e-Oftalmo.CBO: Rev Dig Oftalmol. 2015;1(2):1-2. DOI: 10.17545/e-oftalmo.cbo/2015.18

6. Brody BL, Gamst AC, Williams RA, Smith AR, Lau PW, Dolnak D, et al. Depression, visual acuity, comorbidity, and disability associated with age-related macular degeneration. Ophthalmology. 2001;108(10):1893-900.
7. Borger PH, van Leeuwen R, Hulsman CA, Wolfs RC, van der Kuip DA, Hofman A, et al. Is there a direct association between age-related eye diseases and mortality? The Rotterdam Study. Ophthalmology. 2003;110(7):1292-6.
8. Yuzawa M, Fujita K, Tanaka E, Wang EC. Assessing quality of life in the treatment of patients with age-related macular degeneration: clinical research findings and recommendations for clinical practice. Clin Ophthalmol. 2013;7:1325-32.
9. Wang J, Xue Y, Thapa S, Wang L, Tang J, Ji K. Relation between Age-Related Macular Degeneration and Cardiovascular Events and Mortality: A Systematic Review and Meta-Analysis. Biomed Res Int. 2016;2016:8212063. DOI: 10.1155/2016/8212063.8212063
10. Margolis MK, Coyne K, Kennedy-Martin T, Baker T, Schein O, Revicki DA. Vision-specific instruments for the assessment of health-related quality of life and visual functioning: a literature review. Pharmacoeconomics. 2002;20(12):791-812.
11. Picoto M, Galveia J, Patrício S, Rodrigues A, Vaz F. Qualidade de vida relacionada com a visão em pacientes com degeneração macular relacionada à idade neovascular. Rev Bras Oftalmol. 2015;74(4):216-21.
12. Boyer DS, Heier JS, Brown DM, Francom SF, Ianchulev T, Rubio RG. A Phase IIIb study to evaluate the safety of ranibizumab in subjects with neovascular age-related macular degeneration. Ophthalmology. 2009;116(9):1731-9.
13. CATT Research Group, Martin DF, Maguire MG, Ying GS, Grunwald JE, Fine SL, Jaffe GJ. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. N Engl J Med. 2011;364(20):1897-908.
14. Rayess N, Houston SK 3rd, Gupta OP, Ho AC, Regillo CD. Treatment outcomes after 3 years in neovascular age-related macular degeneration using a treat-and-extend regimen. Am J Ophthalmol. 2015;159(1):3-8.e1.
15. Wykoff CC, Ou WC, Brown DM, Croft DE, Wang R, Payne JF, et al. Randomized Trial of Treat-and-Extend versus Monthly Dosing for Neovascular Age-Related Macular Degeneration. Ophthalmol Retina. 2017;1(4):314-21.
16. Lalwani GA, Rosenfeld PJ, Fung AE, Dubovy SR, Michels S, Feuer W, et al. A variable-dosing regimen with intravitreal ranibizumab for neovascular age-related macular degeneration: year 2 of the PrONTO Study. Am J Ophthalmol. 2009;148(1):43-58.e1.
17. Villegas VM, Aranguren LA, Kovach JL, Schwartz SG, Flynn HW Jr. Current advances in the treatment of neovascular age-related macular degeneration. Expert Opin Drug Deliv. 2017;14(2):273-82.
18. Simão LM, Lana-Peixoto MA, Araújo CR, Moreira MA, Teixeira AL. The Brazilian version of the 25-Item National Eye Institute Visual Function Questionnaire: translation, reliability and validity. Arq Bras Oftalmol. 2008;71(4):540-6.
19. Streiner DL. Being inconsistent about consistency: when coefficient alpha does and doesn't matter. J Pers Assess. 2003;80(3):217-22.
20. Szlyk JP, Pizzimenti CE, Fishman GA, Kelsch R, Wetzel LC, Kagan S, et al. A comparison of driving in older subjects with and without age-related macular degeneration. Arch Ophthalmol. 1995;113(8):1033-40.
21. Dong LM, Childs AL, Mangione CM, Bass EB, Bressler NM, Hawkins BS, et al.; Submacular Surgery Trials Research Group. Health- and vision-related quality of life among patients with choroidal neovascularization secondary to age-related macular degeneration at enrollment in randomized trials of submacular surgery: SST report no. 4. Am J Ophthalmol. 2004;138(1):91-108.
22. Marback RF, Maia OO Jr, Morais FB, Takahashi WY. Quality of life in patients with age-related macular degeneration with monocular and binocular legal blindness. Clinics (Sao Paulo). 2007;62(5):573-8.
23. Williams RA, Brody BL, Thomas RG, Kaplan RM, Brown SI. The psychosocial impact of macular degeneration. Arch Ophthalmol. 1998;116(4):514-20.
24. Tolman J, Hill RD, Kleinschmidt JJ, Gregg CH. Psychosocial adaptation to visual impairment and its relationship to depressive affect in older adults with age-related macular degeneration. Gerontologist. 2005;45(6):747-53.
25. Vanoff SD, Sonn U, Lundgren-Lindqvist B, Steen SB. Disability in daily life activities and visual impairment: a population study of 85-year-old people living at home. Scand J Occup Ther. 2000;7(4):148-55.
26. Backman H, Williams R. Living with age-related macular degeneration. J Vis Impair Blind. 2002;96(5):345-8.
27. Berdeaux GH, Nordmann JP, Colin E, Arnould B. Vision-related quality of life in patients suffering from age-related macular degeneration. Am J Ophthalmol. 2005;139(2):271-9.
28. Hirneiss C, Schmid-Tannwald C, Kernt M, Kampik A, Neubauer AS. The NEI VFQ-25 vision-related quality of life and prevalence of eye disease in a working population. Graefes Arch Clin Exp Ophthalmol. 2010;248(1):85-92.
29. Stein JD, Newman-Casey PA, Mrinalini T, Lee PP, Hutton DW. Cost-effectiveness of bevacizumab and ranibizumab for newly diagnosed neovascular macular degeneration. Ophthalmology. 2014;121(4):936-45.



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